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Claims

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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In re application of :

Kazuhisa HATAKEYAMA : Docket No. 2000-0644A

Serial No. 09/576,715 : Group Art Unit 1655

Filed May 23, 2000 : Examiner B. Forman

METHOD FOR GENE ANALYSIS :

OIPE JC154 JUN 12 2001 PATENT & TRADEMARK OFFICE

THE COMMISSIONER IS AUTHORIZED TO CHARGE ANY DEFICIENCY IN THE FEES FOR THIS PAPER TO DEPOSIT ACCOUNT NO. 23-0975

AMENDMENT

Assistant Commissioner for Patents,
Washington, D.C. 20231

Sir:

Responsive to the Official Action dated January 12, 2001, the time for filing thereto being extended for two months in accordance with the Petition for Extension submitted concurrently herewith, please amend the above-identified application as follows.

In the Specification:

Page 6, replace the paragraph beginning at line 16 with the following paragraph:

B1

In the present invention, the term "double-stranded DNA-binding protein" refers to a protein which binds to chromosome of eucaryote or that of prokaryote strongly and concerns retention of higher-order structure of chromosome. That is, it comprises a protein having function to stabilize a complementary double-stranded DNA.

In the Claims:

Please amend the claims as follows.

1. (Amended) A method of gene analysis by detecting hybridization between a probe nucleic acid and a sample nucleic acid comprising a target sequence complimentary to that of the probe nucleic acid, wherein at least one of the probe nucleic acid and the sample nucleic acid is DNA, said method comprising:

immobilizing either the probe nucleic acid or the sample nucleic acid on a substrate,

adding the other non-immobilized probe nucleic acid or sample nucleic acid to the immobilized probe nucleic acid or sample nucleic acid on the substrate,

promoting hybridization in the presence of a double-stranded DNA-binding protein having a function to stabilize a complementary double-stranded DNA, and

detecting the hybridization.

7. (Amended) The method according to claim 1, wherein the double-stranded DNA-binding protein is a Sso7d protein derived from *Sulfolobus solfataricus.*

8. (Amended) The method according to claim 1, wherein the double-stranded DNA-binding protein has a homology of 75% or more with the amino acid sequence of SED ID NO: 9.

10. (Amended) The method according to claim 9, wherein the amount of the sample nucleic acid comprising the target sequence is analyzed based on the intensity of a hybridization

signal obtained from the hybridization of the labeled sample nucleic acid and the probe nucleic acid.

11. (Amended) The method according to claim 9, wherein the detection of the hybridization is performed by using a plurality of probe nucleic acids and detecting the polymorphism in the target sequence by comparing the intensity of each hybridization signal obtained from the hybridization of the labeled sample nucleic acid and the plurality of probe nucleic acids.

12. (Amended) The method according to claim 9, wherein the detection of the hybridization is performed by using a plurality of probe nucleic acids and detecting nucleotide sequence of the sample nucleic acid by comparing the intensity of each hybridization signal obtained from the hybridization of the labeled sample nucleic acid and the plurality of probe nucleic acids.

13. (Amended) A test kit for detecting hybridization between a probe nucleic acid and a sample nucleic acid comprising a target sequence complementary to that of the probe nucleic acid, which comprises at least a double-stranded DNA-binding protein having a function to stabilize a complementary double-stranded DNA.

REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Initially, Applicant wishes to note that in support of the remarks contained herein below, a Declaration has been submitted along with the response under 37 CFR 1.132.

The specification has been carefully reviewed and editorial changes have been effected. All of the changes are minor in nature and therefore do not require extensive discussion.

Claims 1, 7, 8 and 10-13 have been amended to put the claims in better form under U.S. practice and to address each ground of rejection under 35 U.S.C. § 112, second paragraph. Support for the claim amendments is readily apparent from the teachings of the specification and the original claims (see in particular, pages 6-20 of the specification)

With regard to the rejection of claims 1-12 under 35 USC § 112, second paragraph, Applicant believes that each ground of rejection has been overcome by the amendments to the claims. Specifically, claims 1 and 10-12 have been amended to address each of the Examiner's concerns outlined in item 2 of the January 12, 2001 Official Action. Thus, in light of the amended claims, Applicant respectfully requests that this rejection be withdrawn.

With regard to the rejection of claims 1, 2 and 11-13 under 35 USC § 102(b) as being clearly anticipated by Wagner et al. (WO 93/02216, published 4 February 1993), this rejection is deemed to be untenable and is thus respectfully traversed.

To constitute anticipation of the claimed invention, a single prior art reference must disclose each and every material element of the claim. Here, in this case, Wagner et al. fail to

teach or suggest the presence of a double-stranded DNA-binding protein having a function to stabilize a complementary double-stranded DNA.

As stated in the specficiation, an object of the present invention is to provide a method for gene analysis quickly and with high precision and high sensitivity by performing hybridization in the presence of a double-stranded DNA-binding protein having a function to stabilize a complementary double-stranded DNA. According to the present invention, it is possible to confirm complete homology between a probe nucleic acid and a sample nucleic acid with high precision and high sensitivity using the claimed method.

Wagner et al. disclose a method for detecting a mutation from a non-mutated sequence of a single stranded target polynucleotide in a sample, comprising (a) incubating the sample with a single-stranded polynucleotide hybridization partner comprising at least one single-stranded base sequence which is complementary to the non-mutated sequence of the target polynucleotide to form hybrid; (b) contacting the hybrid formed in step (a) with a mismatch-binding protein; and (c) detecting the presence of any mismatch-binding protein bound to said hybrid; whereby the detection of the presence of the mismatch-binding is indicative of the presence of a mutation in the sequence of the polynucleotide of the sample.

As described above, in the present invention, a double-stranded DNA-binding protein is added ***to confirm complete homology between a probe nucleic acid and a sample nucleic acid***, that is, to perform hybridization quickly and with high sensitivity. In contrast, in the Wagner et al. reference, the DNA mismatch-binding protein is added ***to detect whether there is a mutation or not in a sample***.

Thus, since Wagner et al. fail to teach or suggest each and every material element of the present invention, this rejection can not be sustained and should be withdrawn.

With regard to the rejection of claims 3-10 under 35 USC § 103(a) as being unpatentable over Wagner et al. (WO 93/02216, published 4 February 1993) in view of Guagliardi et al. (Journal of Molecular Biology, 1997, 267: 841-848) and SwisProt (accession No. 059631, 15 December 1998 and accession No. P39476; P81550, 1 February 1995), this rejection is also deemed to be untenable and is thus respectfully traversed.

The Examiner states that "it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the DNA-binding protein in the method of Wagner et al. with the Sso7d protein taught by Guagliardi et al. and Swiss-Prot, which has the known amino acid sequence, for the expected benefit of analyzing genes with reduced time of hybridization, at higher temperatures and with increased specificity". However, for the following reasons, Applicant respectfully disagrees with the Examiner in this regard.

Under U.S. practice, an obviousness rejection based on similarity of methods entails the motivation of one skilled in the art to practice the claimed method, in the expectation that methods similar in steps will have similar results. However, in this case, the method of the present invention is unexpectedly superior to the methods of the cited references.

As shown in the Rule 1.132 Declaration submitted herewith, in the present invention, the combination of immobilizing either a probe nucleic acid or a sample nucleic acid on a substrate and using a double-stranded DNA-binding protein having a function to stabilize a complementary double-stranded DNA makes the hybridization signal intensity stronger and

background lower. As a result, the present invention allows for gene analysis to be performed with high speed and high sensitivity using a plurality of samples.

In contrast, Guagliardi et al. disclose that the characteristics of the protein Sso7d are analyzed by a band shift assay with the electrophoresis method. This method cannot be performed for gene analysis in a high-throughput and high speed manner using a plurality of samples since this method requires a long time for assay and because detection of hybridization is measured by an RI method.

Furthermore, as stated in the arguments above, Wagner et al. teach a DNA mismatch-binding protein to detect whether there is a mutation or not in a sample and not to confirm complete homology between a probe nucleic acid and a sample nucleic acid.

Still further, it is required under U.S. practice that the cited references, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify the teachings of Wagner et al. to arrive at the present invention. Although the Examiner noted that it would have been obvious to a skilled artisan to modify the DNA-binding protein in the method of Wagner et al. with the Sso7d protein taught by Guagliardi et al. and Swiss-Prot for the expected benefit of analyzing genes with reduced time of hybridization, at higher temperatures and with increased specificity, Applicant submit that one skilled in the art based on the teachings of Wagner et al. would not have been motivated to effect such a modification since Wagner et al. ***teaches away*** from such a modification. As stated above, Wagner et al. uses the DNA mismatch-binding protein in their method to detect whether there is a mutation or not in a sample. A double-

stranded DNA-binding protein such as Sso7d having a function to stabilize a complementary double-stranded DNA would prevent Wagner et al. from practicing their disclose method.

Thus, since the combination of Wagner et al., Guagliardi et al. and Swiss-Prot do not render obvious the present invention, this rejection of claims 3-10 under 35 USC § 103(a) cannot be sustained and should be withdrawn.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached pages are captioned **"Version with markings to show changes made."**

In view of the foregoing amendments and remarks, it is respectfully submitted that the Application is now in condition for allowance. Such action is thus respectfully solicited.

If, however, the Examiner has any suggestions for expediting allowance of the application or believes that direct communication with Applicant's attorney will advance the prosecution of this case, the Examiner is invited to contact the undersigned at the telephone number below.

Respectfully submitted,

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